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Dermoscopy Improves Accuracy of Primary Care Physicians to Triage Lesions Suggestive of Skin Cancer

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Ethical approval was not required because this is not a study that "prospectively assigns human subjects to intervention or comparison groups to evaluate the cause-and-effect relationship between a medical intervention and a health outcome." Although the patients were assessed differently by primary care physicians (a group of them using dermoscopy as an additional tool for the clinical screening of skin tumors), the patients' outcome was not affected because all patients were re-evaluated by expert dermatologists who took the responsibility for the final diagnosis and treatment.

All authors declare their independence from those providing funds.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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ABSTRACT

Purpose
Primary care physicians (PCPs) constitute an appropriate target for new interventions and educational campaigns designed to increase skin cancer screening and prevention. The aim of this randomized study was to determine whether the adjunct of dermoscopy to the standard clinical examination improves the accuracy of PCPs to triage lesions suggestive of skin cancer.

Patients and Methods
PCPs in Barcelona, Spain, and Naples, Italy, were given a 1-day training course in skin cancer detection and dermoscopic evaluation, and were randomly assigned to the dermoscopy evaluation arm or naked-eye evaluation arm. During a 16-month period, 73 physicians evaluated 2,522 patients with skin lesions who attended their clinics and scored individual lesions as benign or suggestive of skin cancer. All patients were re-evaluated by expert dermatologists at clinics for pigmented lesions. Referral accuracy of both PCP groups was calculated by their scores, which were compared to those tabulated for dermatologists.

Results
Referral sensitivity, specificity, and positive and negative predictive values were 54.1%, 71.3%, 11.3%, and 95.8%, respectively, in the naked-eye arm, and 79.2%, 71.8%, 16.1%, and 98.1%, respectively, in the dermoscopy arm. Significant differences were found in terms of sensitivity and negative predictive value ($P = .002$ and $P = .004$, respectively). Histopathologic examination of equivocal lesions revealed 23 malignant skin tumors missed by PCPs performing naked-eye observation and only six by PCPs using dermoscopy ($P = .002$).

Conclusion
The use of dermoscopy improves the ability of PCPs to triage lesions suggestive of skin cancer without increasing the number of unnecessary expert consultations.

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INTRODUCTION

Skin cancer is the most common malignancy in whites and accounts for about one third of all cancers diagnosed per year.[1] Melanoma is often lethal but can usually be cured if diagnosed early. Nonmelanoma skin cancer (including basal cell carcinoma [BCC] and squamous cell carcinoma [SCC]) is seldom lethal, but if advanced, can cause severe disfigurement. Early detection and treatment, therefore, is the best strategy to reduce mortality and morbidity associated with melanoma and nonmelanoma skin cancers, respectively.

The clinical diagnosis of skin cancer is based on several morphologic features pertaining to the shape, elevation, surface, and color of the tumor. The simple morphologic features summarized by the asymmetry, border irregularity, color variegation, and diameter > 5 mm (ABCD) rule are currently widely used for diagnosing skin cancer, particularly melanoma.[2] However, ABCD criteria achieve only 65% to 80% sensitivity.[3] The ABCD rule fails to recognize melanomas that are small (< 6 mm)[4] or that exhibit regular shape and homogeneous color. On the other hand, a variety of benign pigmented skin lesions mimic melanoma clinically, resulting in unnecessary excisions.

For diagnosis of skin cancer, dermoscopy has been shown to be more accurate than naked-eye examination because dermoscopy allows the visualization of features that are not visible to the naked eye.[5,6] Dermoscopy is currently used by experienced clinicians as a second-level procedure for the evaluation of selected lesions that were considered suggestive of skin cancer by the initial clinical examination.[7,8] Under these circumstances, dermoscopy

has been shown to decrease the number of unnecessary excisions of benign lesions.[9,10] However, no studies have been reported that evaluate the impact of dermoscopy as a diagnostic tool for primary care physicians (PCPs) in a first-level evaluation of nonselected skin tumors. In this setting, the primary purpose of dermoscopy could simply be to determine whether a lesion needs to undergo a more detailed evaluation by experienced clinicians.

To help PCPs use dermoscopy to assess skin tumors and determine which patients should be given referrals to specialists, we developed a simplified diagnostic algorithm, known as the three-point checklist, based on the evaluation of three dermoscopic criteria. In an earlier study, this algorithm showed good reproducibility and high sensitivity in the hands of dermoscopy novices.[11]

The aim of this prospective randomized study was to determine whether PCPs achieve greater accuracy to triage skin lesions suggestive of skin cancer using dermoscopic evaluation and the three-point checklist in addition to the standard clinical examination.

PATIENTS AND METHODS

This study was conducted in Naples, Italy, and in Barcelona, Spain. The study design consisted of four steps (Fig 1). In step 1 (PCP recruitment and training), PCPs were selected and given training in identification of skin cancer using the ABCD rule and the three-point checklist. In Naples, PCPs from different geographic areas of the city were invited to participate. In Barcelona, PCPs were recruited from two of the largest healthcare cooperatives (see Appendix). Only the PCPs who attended the training sessions and who subsequently screened patients and referred them to the Pigmented Lesion Clinics (PLCs) were considered participants in the study.

Two identical 1-day training courses (one in Naples and one Barcelona) were organized for the PCPs. Each course was subdivided in two sessions of 2 hours each. The first part described the ABCD rule for the clinical diagnosis of melanoma and the basic clinical criteria for the recognition of nonmelanoma skin cancers, including BCC and SCC. The second part described the three-point checklist, which is a simple dermoscopic algorithm for distinguishing benign and malignant tumors.[11] This algorithm is based on the recognition of only three individual features: dermoscopic asymmetry (in color and/or structure, not in shape), atypical network (pigmented network with thick lines and irregular distribution), and blue-white structures (presence of any blue and/or white color within the lesion). For the three-point checklist, the presence of two or more features suggests malignancy (Fig 2).

In step 2 (PCP allocation and patient screening), the PCPs who completed the training course were randomly assigned to an arm in which lesions were evaluated by standard clinical examination or to an arm in which dermoscopy was used in addition to the naked-eye assessment of skin tumors. PCPs assigned to the dermoscopy arm were given a hand-held dermatoscope (Dermlite; 3Gen LLC, Dana Point, CA).

After the PCPs were assigned to an evaluation arm, consecutive patients asking for screening or exhibiting one or more skin tumors, as seen by the PCPs at a routine physical examination (patient-finding screening), were considered for inclusion. In each geographic area, each PCP in both groups examined the individual lesions and scored the patient outcome, as banal or suggestive of skin cancer, on a form that included an anonymous identification code indicating the referring PCP, the age and sex of the patient, and the locations of the lesions.

In step 3 (expert evaluation), all patients were re-evaluated by at least two melanoma experts in each of two PLCs involved in the study (one in Naples and one in Barcelona). The individual lesions were evaluated and scored as banal or suggestive of skin cancer by the experts who were blinded with respect to the evaluation arm of the referring PCP.

In step 4 (excision and histopathology), all lesions that were considered suggestive of skin cancer at PLC were excised and subsequently diagnosed histopathologically. Equivocal lesions by histopathologic examination were reviewed by a second independent pathologist (D.M.) and a final diagnosis was made.

Diagnostic accuracy refers to the ability of a physician to identify correctly a lesion as malignant or benign when the gold standard is the histopathologic examination. Referral accuracy refers to the ability of a physician to correctly

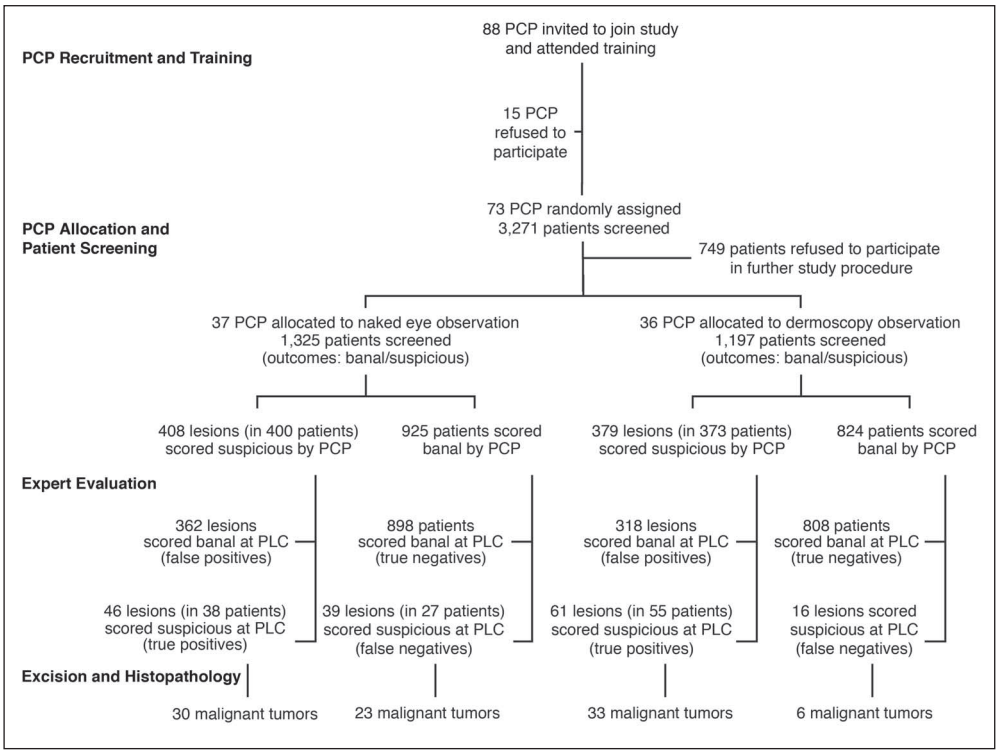

Fig 1. Flow diagram summarizing the study procedure. PCP, primary care physician; PLC, pigmented lesion clinic.

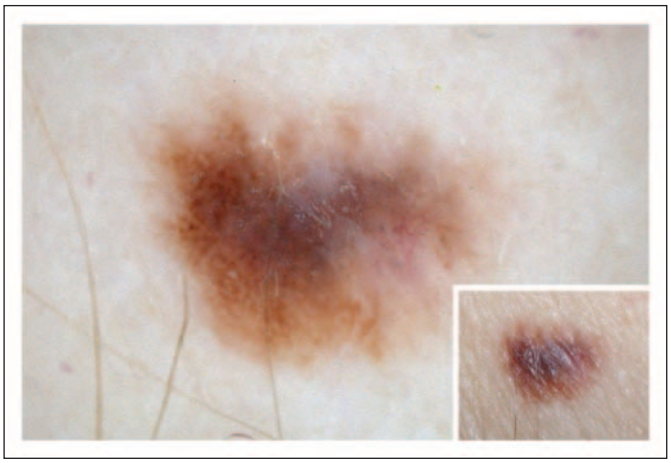

Fig 2. Early melanoma (0.7 mm in thickness) exhibiting only slight asymmetry by naked eye examination (inset). Dermoscopic observation reveals striking asymmetry in color and structure, atypical pigment network (left side of the lesion), and blue-white structures (in the center and right side). The lesion was thus scored suggestive of skin cancer by the primary care physician.

determine that a lesion may be malignant or benign when the gold standard is diagnosis by a second expert clinician.[12] Given that the aim of our study was to verify the ability of PCPs to identify lesions suggestive of skin cancer for referral for a second expert opinion, the evaluation performed at PLCs was chosen as the gold standard. Referral accuracy (in terms of sensitivity, specificity, and positive and negative predictive values) was thus calculated on the basis of contingency tables between outcomes (banal/suggestive of skin cancer) of PCP diagnoses and outcomes (excision yes/no) of diagnoses by experts at the PLCs.

Unless otherwise indicated, diagnostic measures are calculated by numbers of patients, given that the occurrence of more than one lesion judged to be excised in a single patient is a rare event.[13] Patients who had been considered for inclusion by PCPs but did not attend the PLC for re-evaluation were not included in the analysis.

Differences between the two evaluation arms were tested using *t* test and χ^2 test. Regarding prevalence of lesions suggestive of skin cancer (as judged by PLCs and PCPs) and prevalence of benign and malignant tumors, as diagnosed histopathologically, the differences between the two arms were tested against the null hypothesis of an odds ratio = 1. Given the cluster randomized design, the correlation of responses of each PCP was therefore accounted for by applying the method of generalized estimating equations with robust estimates of the variance and covariance of estimated coefficients.[14] The same marginal regression modeling framework was used to calculate points and intervals estimates and differences between the two arms in terms of sensitivity, specificity, and positive and negative predictive values.[15]

RESULTS

Eighty-eight PCPs (52 from Naples and 36 from Barcelona) attended the training workshops, and 73 PCPs (40 from Naples and 33 from Barcelona) participated fully in the study. Of these, 37 were assigned to the naked-eye evaluation arm, and 36 to the dermoscopy evaluation arm.

The study population consisted of 2,522 patients observed during a period of 16 months (May 2003 to September 2004). Seven hundred forty-nine patients who were considered for inclusion by the PCP but were lost for the re-evaluation at the PLC, were not included in the study. As shown in Table 1, patients were equally distributed in the two arms of the study (naked-eye and dermoscopy evaluation) in terms of age, sex, and prevalence of lesions suggestive of skin cancer as judged at the PLCs. Hence, randomization seemed to reach a homogeneous confounder distribution among groups.

About one third of the patients in both arms had lesions scored as suggestive of skin cancer by PCPs (30.3% naked-eye and 31.5% dermoscopy; $P = .787$), whereas only approximately 6% of all patients had lesions considered suggestive of skin cancer at PLCs (6.3% naked eye and 6.4% dermoscopy arm; $P = .886$). This number of lesions falsely assessed as suspicious by PCPs was responsible for the relatively low positive predictive value achieved by PCPs in both arms (Table 1): 11.3% (naked-eye examination) to 16.1% (dermoscopy examination) of patients referred by PCPs as having lesions suggestive of skin cancer were indeed judged equivocal at PLC ($P = .106$). However, 71.3% (naked-eye arm) and 71.8% (dermoscopy arm) of patients with banal lesions were correctly identified by PCPs (specificity; $P = .915$), with negative predictive values of 95.8% and 98.1% in the naked-eye and

Table 1. Patient Demographics and Referral Accuracy by Evaluation Group

Characteristic	Naked-Eye Evaluation Group	Dermoscopy Evaluation Group	*P*
No. of lesions	1,345 (in 1,325 patients)	1,203 (in 1,197 patients)	—
Age of patients, years			.502*
Mean	40	41	
Range	2-90	3-94	
Females	827	746	.962†
%	62.4	62.3	
Prevalence of lesions suggestive of skin cancer, %	6.3	6.4	.886‡
Sensitivity	54.1	79.2	.002‡
95% CI	46.3-61.7	66.9-87.8	
Specificity	71.3	71.8	.915‡
95% CI	65.6-76.4	64.1-78.3	
Positive predictive value	11.3	16.1	.106‡
95% CI	8.5-14.8	11.4-22.2	
Negative predictive value	95.8	98.1	.004‡
95% CI	94.4-96.9	96.8-98.8	

*t test.
†χ^2 test.
‡Generalized estimating equation (logit).

dermoscopy arms, respectively ($P = .004$). This means that there was a low probability that PCPs, especially in the dermoscopy arm, would fail to refer a patient with a lesion suggestive of skin cancer for a second expert opinion.

Although the two arms did not differ significantly in specificity, the dermoscopy arm scored significantly higher in sensitivity than did the naked-eye arm ($P = .002$). Patients with lesions suggestive of skin cancer were identified correctly in 79.2% of cases in the dermoscopy arm, compared with 54.1% of cases in the naked-eye arm (Table 1).

As shown in Figure 1 and Table 2, 162 lesions judged to be suggestive of skin cancer by the experts at PLCs were excised for histopathologic examination. One-hundred nineteen patients underwent excision of one lesion each; nine patients had two lesions excised; seven patients had three lesions excised, and one patient had four lesions excised. Histopathologically, there were no significant differences in terms of prevalence of benign and malignant tumors in the two evaluation arms (Table 2). Among the overall population screened, melanoma and the overall number of malignant tumors (including melanoma, BCC, and SCC) showed prevalence of 0.5% and 3.6%, respectively. Among all patients with lesions considered suggestive of skin cancer by PCPs, melanoma and the overall number of malignant tumors exhibited prevalence of 1.5% and 11.7%, respectively. Of 12 melanomas identified in this study, seven were in situ, four were early invasive (Breslow thickness < 0.75 mm), and one was thick melanoma (Breslow thickness of 6 mm).

As shown in Figure 1 and Table 3, a similar number of histopathologically proven malignant tumors were identified by the PCPs in the naked-eye and dermoscopy arms (30 and 33 lesions, respectively). Conversely, 23 malignant tumors (18 BCC, three SCC, and two melanomas [one in situ and one 6 mm thick]) were missed by PCPs performing naked-eye observation, compared with only six missed by PCPs using dermoscopy (four BCC, one SCC, and one melanoma 0.7 mm thick; $P = .002$).

Table 3. No. of Malignant Tumors As Diagnosed by Histopathologic Examination, by Outcome Scored by Primary Care Physician

Lesion Type	Naked-Eye Evaluation Group		Dermoscopy Evaluation Group	
	Banal Lesion	Lesion Suggestive of Skin Cancer	Banal Lesion	Lesion Suggestive of Skin Cancer
Overall malignant tumors	23	30	6	33
Basal cell carcinoma	18	19	4	25
Squamous cell carcinoma	3	7	1	3
Melanoma	2	4	1	5

DISCUSSION

The most significant result of this randomized trial is that the use of dermoscopy allowed PCPs to perform 25.1% better triage of skin lesions suggestive of skin cancer compared with naked-eye examination alone ($P = .002$). PCPs using dermoscopy performed significantly better also in terms of negative predictive value ($P = .004$), resulting in a low risk (1.9%) for patients with lesions suggestive of skin cancer not to be referred by PCPs for a second expert opinion.

Approximately 40% of office visits to physicians, at least in the United States, are to a family practitioner or internist,[16] and almost all physician-detected melanomas are discovered by PCPs rather than by specialists.[17] Compared with family or self-detection, physician detection is associated with an increased probability of diagnosing thinner melanomas.[18] However, although most melanoma patients have at least one primary care visit in the year before diagnosis, only 20% report receiving a skin cancer examination.[17] PCPs, therefore, are in a unique position to perform skin cancer screening, and constitute the appropriate target for new interventions and educational campaigns designed to increase skin cancer screening and prevention.

Given that the aim of our study was to assess the ability of PCPs to identify lesions suggestive of skin cancer for referral, the evaluation performed at PLCs was chosen as the gold standard. PCPs performing standard clinical examination had referral sensitivity and specificity of 54.1% and 71.3%, respectively. These rates are similar to those reported previously.[13,19] By adding dermoscopy to the standard clinical examination, PCPs achieved significantly better referral sensitivity (from 54.1% to 79.2%; $P = .002$). The latter result occurred without a decrease in specificity (71.8%), suggesting that better triage of possible malignant skin tumors could occur without increasing the number of unnecessary expert consultations. Similar results have also been reported in a previous study based on the evaluation of clinical and dermoscopic pictures performed by a group of 74 PCPs.[20] In the latter study, PCP who attended a brief dermoscopy training session

Table 2. No. of Benign and Malignant Tumors As Diagnosed by Histopathologic Examination, by Evaluation Group

Lesion Type	Naked-Eye Evaluation Group (n = 1,345)		Dermoscopy Evaluation Group (n = 1,203)		Overall (n = 2,548)		
	No.	%	No.	%	No.	%	GEE (logit) *P*
Overall malignant tumors	53	3.9	39	3.2	92	3.6	.692
Melanoma	6	0.4	6	0.5	12	0.5	.778
Basal cell carcinoma	37	2.8	29	2.4	66	2.6	.787
Squamous cell carcinoma	10	0.7	4	0.3	14	0.5	.256
Overall benign tumors	32	2.4	38	3.2	70	2.7	.396
Melanocytic nevi	22	1.6	29	2.4	51	2.0	.339
Seborrheic keratosis	6	0.4	7	0.6	13	0.5	.819
Other benign lesions	4	0.3	2	0.2	6	0.2	.537

Abbreviation: GEE, generalized estimating equation.

achieved improved sensitivity without a decrease in specificity for the diagnosis of melanoma compared with a control group.

In our study, PCPs who performed dermoscopic examination after a brief training course had better results in both positive and negative predictive values (16.1% and 98.1%, respectively) than did PCP performing naked-eye examination (positive predictive value, 11.3%; negative predictive value, 95.8%). It is noteworthy that a relatively low positive predictive value (13.7%) has also been reported in an expert setting (PLCs) where diagnostic accuracy was tested in a population with a relatively low prevalence of melanoma.[21]

Interestingly, the dermoscopy algorithm taught to PCPs in our study, namely the three-point checklist, was originally developed for differentiation of pigmented skin tumors.[11] However, a considerable number of nonmelanoma skin cancers, including nonpigmented lesions, were correctly identified by the PCPs using dermoscopy. Thus, it could be speculated that the increased dedication of PCPs to the patients, a sine qua non condition to perform dermoscopy, was in itself one of the main reasons for the increased detection of suspected skin malignancies.

A good skin-cancer screening test should be available to all individuals with skin tumors to identify those who are at high risk for skin cancer. We propose that dermoscopy be used in clinical management of patients with skin tumors as a first-line screening tool. Dermoscopy is a valid, simple, and safe method for PCPs to identify high-risk lesions that require further examination by experts. As a first-level screening tool, dermoscopy may help PCPs in performing better detection of skin tumors suggestive of skin cancer (increased referral sensitivity), as demonstrated in this study. As a second-level procedure for clinically equivocal lesions, dermoscopy performed by expert clinicians can reduce the number of unnecessary excisions of benign lesions (better specificity than naked-eye examination), as previously demonstrated.[9,10]

Evidence is lacking that skin examination for cancer screening is effective in reducing mortality or morbidity from skin tumors.[22] However, it has also been claimed that "no one should die of malignant melanoma"[23] because "melanoma writes its message on the skin with its own ink, and it is there for all to see."[24] Dermoscopy may help clinicians to better recognize this ink.

REFERENCES

1. Jemal A, Tiwari RC, Murray T, et al: Cancer statistics, 2004. CA Cancer J Clin 54:8-29, 2004

2. Friedman RJ, Rigel DS, Kopf AW: Early detection of malignant melanoma: The role of physician examination and self-examination of the skin. CA Cancer J Clin 35:130-151, 1985

3. Grin CM, Kopf AW, Welkovich B, et al: Accuracy in the clinical diagnosis of malignant melanoma. Arch Dermatol 126:763-766, 1990

4. Heymann WR: Clinical and microscopic diagnosis of melanoma. J Am Acad Dermatol 52:133-134, 2005

5. Argenziano G, Soyer HP: Dermoscopy of pigmented skin lesions: A valuable tool for early diagnosis of melanoma. Lancet Oncol 2:443-449, 2001

6. Argenziano G, Soyer HP, Chimenti S, et al: Dermoscopy of pigmented skin lesions: Results of a consensus meeting via the Internet. J Am Acad Dermatol 48:679-693, 2003

7. Bafounta ML, Beauchet A, Aegerter P, et al: Is dermoscopy (epiluminescence microscopy) useful for the diagnosis of melanoma? Results of a meta-analysis using techniques adapted to the evaluation of diagnostic tests. Arch Dermatol 137:1343-1350, 2001

8. Kittler H, Pehamberger H, Wolff K, et al: Diagnostic accuracy of dermoscopy. Lancet Oncol 3:159-165, 2002

9. Carli P, de Giorgi V, Chiarugi A, et al: Addition of dermoscopy to conventional naked-eye examination in melanoma screening: A randomized study. J Am Acad Dermatol 50:683-689, 2004

10. Carli P, De Giorgi V, Crocetti E, et al: Improvement of malignant/benign ratio in excised melanocytic lesions in the 'dermoscopy era': A retrospective study 1997-2001. Br J Dermatol 150:687-692, 2004

11. Soyer HP, Argenziano G, Zalaudek I, et al: Three-point checklist of dermoscopy: A new screening method for early detection of melanoma. Dermatology 208:27-31, 2004

12. Chen SC, Bravata DM, Weil E, et al: A comparison of dermatologists' and primary care physicians' accuracy in diagnosing melanoma: A systematic review. Arch Dermatol 137:1627-1634, 2001

13. Carli P, De Giorgi V, Nardini P, et al: Melanoma detection rate and concordance between self-skin examination and clinical evaluation in patients attending a pigmented lesion clinic in Italy. Br J Dermatol 146:261-266, 2002

14. Klar N, Donner A: Current and future challenges in the design and analysis of cluster randomization trials. Stat Med 20:3729-3740, 2001

15. Leisenring W, Pepe MS, Longton G: A marginal regression modelling framework for evaluating medical diagnostic tests. Stat Med 16:1263-1281, 1997

16. Oliveria SA, Christos PJ, Marghoob AA, et al: Skin cancer screening and prevention in the primary care setting: National ambulatory medical care survey 1997. J Gen Intern Med 16:297-301, 2001

17. Geller AC, Koh HK, Miller DR, et al: Use of health services before the diagnosis of melanoma: Implications for early detection and screening. J Gen Intern Med 7:154-157, 1992

18. Epstein DS, Lange JR, Gruber SB, et al: Is physician detection associated with thinner melanomas? JAMA 281:640-643, 1999

19. Osborne JE, Chave TA, Hutchinson PE: Comparison of diagnostic accuracy for cutaneous malignant melanoma between general dermatology, plastic surgery and pigmented lesion clinics. Br J Dermatol 148:252-258, 2003

20. Westerhoff K, McCarthy WH, Menzies SW: Increase in the sensitivity for melanoma diagnosis by primary care physicians using skin surface microscopy. Br J Dermatol 143:1016-1020, 2000

21. Carli P, Nardini P, Crocetti E, et al: Frequency and characteristics of melanomas missed at a pigmented lesion clinic: A registry-based study. Melanoma Res 14:403-407, 2004

22. Helfand M, Mahon SM, Eden KB, et al: Screening for skin cancer. Am J Prev Med 20:47-58, 2001

23. Ackerman AB: No one should die of malignant melanoma. J Am Acad Dermatol 12:115-116, 1985

24. Davis N: Modern concepts of melanoma and its management. Ann Plast Surg 1:628-629, 1978

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Appendix

The Appendix is included in the full-text version of this article, available online at www.jco.org. It is not included in the PDF version (via Adobe® Reader®).

Authors' Disclosures of Potential Conflicts of Interest

Although all authors completed the disclosure declaration, the following authors or their immediate family members indicated a financial interest. No conflict exists for drugs or devices used in a study if they are not being evaluated as part of the investigation. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

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